MANTER: Journal of Parasite Biodiversity (ISSN 2470-8224)
Occasional Papers, Number 23, October 27, 2022
doi: 10.32873/unl.dc.manter23
https://digitalcommons.unl.edu/manter/
Copyright © 2022 Orsolya Molnár, Eric P. Hoberg, Valeria Trivellone, Gábor Földvári, and Daniel R. Brooks

This article has been produced in support of and with appreciation for the efforts by Gábor Földvári of the Institute of Evolution, Centre for Ecological Research, and the Centre for Eco-Epidemiology, National Laboratory for Health Security (both located at 1121 Budapest, Konkoly-Thege Miklós út 29-33, Hungary). Through his untiring efforts, team building, and leadership, he has secured the first EU-wide team research grant. This work was supported by the National Research, Development and Innovation Office in Hungary (RRF-2.3.1-21-2022-00006) and the COST Action CA21170 "Prevention, anticipation and mitigation of tick-borne disease risk applying the DAMA protocol (PRAGMATICK)," which represent the first funded efforts to apply the principles of the DAMA protocol.

The 3P Framework: A Comprehensive Approach to Coping with the Emerging Infectious Disease Crisis

Orsolya Molnár,[1,2] Eric Hoberg,[3,4] Valeria Trivellone,[5] Gábor Földvári,[2] and Daniel R. Brooks[2,6,7,8]

1 Konrad Lorenz Institute for Evolution and Cognition Research, Vienna, Austria
2 Eötvös Loránd Research Network, Centre for Ecological Research, Institute for Evolution, Budapest, Hungary
3 Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin–Madison, Madison, Wisconsin, USA
4 Museum of Southwestern Biology, Department of Biology, University of New Mexico, Albuquerque, New Mexico, USA
5 Illinois Natural History Survey, Prairie Research Institute, University of Illinois at Urbana-Champaign, Champaign, Illinois, USA
6 Stellenbosch Institute for Advanced Study, Stellenbosch, South Africa
7 Harold W. Manter Laboratory of Parasitology, University of Nebraska State Museum, University of Nebraska–Lincoln, Lincoln, Nebraska USA
8 Department of Ecology and Evolutionary Biology, University of Toronto, Toronto, Ontario, Canada

Corresponding author – Orsolya Molnár, Konrad Lorenz Institute for Evolution and Cognition Research, Martinstrasse 12, Klosterneuburg, Austria, 3400, email orsolya.bajer-molnar@kli.ac.at

Abstract

The COVID-19 pandemic is the latest example of the profound socioeconomic impact of the emerging infectious disease (EID) crisis. Current health security measures are based on a failed evolutionary paradigm that presumes EID is rare and cannot be predicted because emergence requires the prior evolution of novel genetic capacities for colonizing a new host. Consequently, crisis response through preparation for previously emerged diseases and palliation following outbreaks have been the only health security options, which have become unsustainably expensive and unsuccessful. The Stockholm paradigm (SP) is an alternative evolutionary framework that suggests host changes are the result of changing conditions that bring pathogens into contact with susceptible hosts, with novel genetic variants arising in the new host after infection. Host changes leading to EID can be predicted because preexisting capacities for colonizing new hosts are highly specific and phylogenetically conservative. This makes EID prevention through limiting exposure to susceptible hosts possible. The DAMA (Document, Assess, Monitor, Act) protocol is a policy extension of the SP that can both prevent and mitigate EID by enhancing traditional efforts through adding early warning signs and predicting transmission dynamics. Prevention, preparation, and palliation compose the 3P framework, a comprehensive plan for reducing the socioeconomic impact of EID.

Keywords: emerging infectious diseases, Stockholm paradigm, DAMA protocol, prevention strategies, public health, global health security

The Emerging Infectious Diseases Crisis

The last fifty years have seen some of the most significant technological and scientific advancements in history. This period also coincides with the crisis of emerging infectious diseases (EIDs) (Brooks and Ferrao, 2005; Rohde, 2013). Technological advancements produce unanticipated ecological disruptions through (1) human intrusion into natural ecosystems and (2) creation of artificial habitats suitable for rapid spread of particular pathogens, sometimes called industrial pathology (Breiman, 1996; Foster et al., 2021). Since the 1970s, more than 40 EIDs and more than 1,100 epidemics have been documented in humans. Among those were the 2003 SARS outbreak in Toronto, which had the potential of pandemic development and also revealed how epidemics foster and amplify social tensions between ethnic minorities even within developed countries and high-income populations, in this case involving the marginalization of the Asian-Canadian community (Jacobs, 2007). The 2015 Zika outbreak was one of a series of emergences of this disease that had swept through Africa, Asia, and the Americas, affecting those with limited access to health care services, especially women deprived of reproductive health services (Plourde and Bloch, 2016). Concurrently, an Ebola epidemic disproportionately affected disadvantaged populations across Liberia, Sierra Leone, and Guinea (Burkle and Burkle, 2015), which lacked public health and physical infrastructures.

EIDs affecting livestock and crops also have substantial economic and social impacts (Brooks et al., 2022; Trivellone et al., 2022). Avian influenza has a mortality rate in domestic poultry of 90%–100% within 48 hours of infection (Centers for Disease Control and Prevention, 2022). The 2014–15 avian influenza pandemic affected more than 45 million birds in the US alone, resulting in poultry export bans across 75 countries and the doubling of egg prices within a few weeks (Newton and Kuethe, 2015). The 2018–19 African swine fever (ASF) pandemic resulted in the culling of nearly 20% of Vietnam's pig population, representing almost 6 million animals. China suffered an economic loss of US$141 billion by September 2019 directly due to the bans on international trade and led to the collapse of half of what was the world's pork export market prior to the outbreak (FAO, 2019). Among those emerging in crops, coconut lethal yellowing (LY) is a fatal disease of several species of palms (Martinez and Roberts, 1967) that has severe repercussions on local cultures for which coconuts provide economic security (Gurr et al., 2016). LY destroyed 95% of the coconut palms in a single region in Mexico in only two decades, millions of coconut trees that provided a livelihood for more than 30,000 rural families in Nigeria by 2010, and almost 99% of tall palms and 72% of dwarfs in West Africa by 2006 (Datt et al., 2020).

Prior to the COVID pandemic, treatment costs and production losses due to EIDs of all kinds reached US$1 trillion per year globally (Brooks et al., 2019). Apart from short-term impacts, EIDs produce long-lasting negative social effects, mostly affecting marginalized and/or low-income communities (Leach and Dry, 2010). In addition to more than 200 million confirmed cases and more than 4.3 million deaths, the first six months of the COVID-19 pandemic catalyzed the greatest unemployment rate and economic deflation since World War II (ILO, 2021). Household expenditures were elevated due to medical expenses, and incomes dropped as much 50% (WHO and World Bank, 2019). Healthcare infrastructure was overwhelmed, leading to decreased accessibility for low income, vulnerable groups; at the same time, food insecurity rose and access to education was reduced (Blacke and Wadhwa, 2020).

The EID crisis calls for a reevaluation of current disease management approaches that focus only on managing EIDs after they have emerged (Evans, 2010; Hadler et al., 2015; Apari et al., 2019). Health services are constantly and unpleasantly surprised by each apparently unexpected EID, and these services are then forced into expensive and time-consuming crisis response. Global health systems are backed into a corner, trying to plan protective measures against opponents they know nothing about until they announce themselves.

Approaches to Coping with Emerging Infectious Disease

Disease has been a constant challenge for modern humanity since the early Holocene, when human settlement created highly dense populations that lived in close proximity with domesticated animals. Infections differing in virulence, transmission dynamics, and persistence have influenced human history, from the emergence of sporadic cases of mysterious symptoms to the decimation of human populations of entire regions (see review in Lakoff, 2017). Humanity has therefore always tried to establish an appropriate response to combat diseases, designing actions based on the often limited knowledge that was available.

Palliate: Medicate, Vaccinate

The oldest tradition for combating diseases is palliation, treating and curing those infected and alleviating signs and symptoms of an infection, with the immediate aim of improving patients' life quality and the longer-range

aim of reducing mortality and morbidity. Hygienic restrictions and regulations were among the first palliative measures first introduced in health care facilities by pioneering physicians such as Ignaz Semmelweiss (Bowden et al., 2003; Lane et al., 2010). The medical tools involved in palliation compose two major functional groups: (1) Medication refers to interfering with pathological physiological and/or biochemical pathways of patients or reproducing pathogens within. Although certain medicaments are available for use as prophylaxis for a limited period of time, the majority of application is linked to a prior development of a disease. (2) Vaccination, on the other hand, aims to reduce the morbidity, mortality, and/or incidence number of a known communicable disease by triggering a mild immune response through administering whole or partial pathogens as an antigen (Bowden et al., 2003).

Although they originated before pathogenic agents were known, today's medical practices still include multiple treatment options that target the physiological pathway responsible for the symptoms and not the pathogen itself. Palliation to a large extent has continued as the backbone of combating infectious disease because most infectious diseases are not deemed predictable and thus not preventable.

Global inequality in access to palliative medicine led to the founding of organizations such as Médecins Sans Frontières (MSF, n.d.), an international network that brings medical professionals to treat diseases such as malaria, yellow fever, dengue, hepatitis, or cholera in developing countries and develops educational programs to improve health care infrastructure. The Bill and Melinda Gates Foundation supports research initiatives and medical intervention programs that target inequality, poverty, and health care development in developing countries (Bill & Melinda Gates Foundation, n.d.).

Once humans discovered that particular disease signs and symptoms were caused by infection with particular pathogens, palliation could be made easier by maintaining high standards of hygiene in health care settings and preparing for infectious diseases by having appropriate health care facilities as well as medications and vaccinations on hand. Also, understanding the transmission dynamics of particular infectious pathogens allowed clinicians and public health workers to prepare by anticipating where and at what time of year certain infectious diseases would occur. Ironically, assumptions about seasonality contributed to notions about apparent disappearance of pathogens at local to regional scales when diseases were not observed in circulation. These notions persist, despite J.R. Audy's groundbreaking observation in 1958 that distribution of a pathogen is always broader than the disease it causes (Audy, 1958). These measures set the foundation for modern public health initiative and infrastructure to prepare for infectious disease outbreaks.

Prepare: Stockpile and Eradicate

The late 20th century saw large-scale outbreaks of infectious diseases that affected social structure, economic processes, and industrial production. Starting with the 1976 influenza epidemic, followed by an outbreak of both seasonal (in 2003) and avian influenza (in 2005) that affected poultry production, disease management became an issue of national security (Lakoff, 2017). Medical intervention then needed to be planned using risk assessment metrics and national distribution networks, sparking close collaboration between public health and other sectors such as the pharmaceutical industry, military, and government agencies and the development of new methods, such as scenario-based exercises to estimate the severity of the threat and improve "response strategies" (Johns Hopkins Center for Civilian Biodefense Studies et al., 2001). Intersectoral collaborations led to international alliances (e.g., International Health Regulations (WHO, 2005)), providing further insight into the behavior of known pathogens. Monitoring stations and surveillance networks established in tropical ecosystems fed information into global databases (e.g., Global Influenza Surveillance and Response System (GISRS) (GISRS, n.d.), Global Outbreak Alert and Response Network (GOARN) (GOARN, n.d.), Global Early Warning System (GLEWS) (FAO et al., 2006)) to spot early onset and instigate timely crises response.

Collaborative networks of veterinarians, physicians, and public health experts have been established since the early 1900s, but the EID crisis gave impetus to creating global initiatives. The One Health initiative (AVMA, 2008) was established in 2006 to target vectors and detect reservoirs of known pathogens. Partly in response to the 2003 avian flu pandemic (Burns et al., 2008), the PREDICT project was launched in 2009 as part of USAID's Emerging Pandemic Threats Program to anticipate future pandemics. The Wildlife (Preservation) Trust renamed itself the EcoHealth Alliance (EcoHealth Alliance, n.d.) and joined forces with the PREDICT project in 2010 to study suspected vectors in areas highly affected by malaria, yellow fever, hepatitis, and dengue. Efforts to prepare for EID now include activities as diverse as studies of zoonoses, campaigns for wildlife vaccination, and distribution of insecticides and mosquito nets. Programs aimed at local communities involve establishing education programs, distributing insecticides, procuring equipment to treat the sick in local health care facilities, and initiating mass vaccination programs to mitigate effects.

Once the transmission dynamics of particular pathogens were known, preparation to cope with infectious disease began to include plans to modify the landscape in ways that would disrupt pathogen transmission, mitigating the severity of outbreaks.

Why Palliate and Prepare Are Not Sufficient

Despite growing awareness of the severity of the EID crisis and efforts to prepare better for coping with EIDs, the new millennium saw a concerning increase in the number of previously unknown pathogens that had no previous record of infecting humans (e.g., SARS, MERS, Hepatitis D, COVID-19) and previously known infections either manifesting novel symptoms (e.g., Zika, West Nile virus) or developing resistance to applied treatment (e.g., resistant malaria, MRSA). Each emergence triggered augmented crisis response, but during the time it took for them to take effect, the disease had exacted a toll on the affected countries. Preparation alone had two substantial soft spots: (1) all preparations were based on the assumption that any outbreaks would be caused by known pathogens and (2) EID are emerging far more rapidly than expected.

As for data availability, pathogens considered by preparatory programs had all been established in human communities, and vectors had been detected. However, data availability is often a crucial shortcoming from otherwise highly publicized and documented outbreaks. Specimens are not collected and/or stored under conditions that allow for long-term preservation, taxonomy is often unclear and generic names inhibit performing accurate phylogenetic analyses, or collections were not made and therefore are simply not available for further research (Colella et al., 2021). Crisis response works well in preparation for reemergence of known pathogens, but it is not prevention. Crisis response was designed to combat diseases we have previously been exposed to and have information about from previous outbreaks. The ongoing SARS-CoV-2 pandemic has led to calls for developing a way of preventing the next emergence, but most publications on the subject suggest strengthening, increasing, and improving our response strategies (Khoo and Lantos, 2020; WHO, 2020; DeSalvo et al., 2021; Stenseth et al., 2021) However, when faced with a novel pathogen, crisis response always lags behind the sweeping epidemic (Audy, 1958; Brooks et al., 2020). With EID increasing at an unprecedented rate since the 1970s (WHO, 2007), global health security demands that we acknowledge the limitations of crisis response and add another pillar of disease control: prevention.

The main reason prevention has not been a focus of disease management is the way most scientists perceive relationships between pathogens and their hosts. The traditional paradigm assumes that pathogen attributes are strongly selected, resulting in specialized associations with a narrow range (often assumed to be a single species) of hosts. As a result of such specialization, pathogens are assumed to lose their ability to utilize (infect) novel hosts, and any new colonization (emergent disease) must be preceded by the pathogen evolving new capacities (Parrish and Kawaoka, 2005). The assumption is that, given that such new capacities evolve rarely and at random with respect to any particular potential host, emergence is assumed to be rare and unpredictable, thus prevention is in vain. This traditional paradigm, the core of the standard model for pathogens and disease, fails on three counts: (1) it claims pathogens are tightly co-adapted to a restricted range of hosts, based on assumptions lacking empirical support; (2) it claims that EIDs ought to be rare, whereas they are common, as evidenced by the current EID crisis and by phylogenetic studies showing that host colonization has been common throughout evolutionary history; and (3) it claims that host switching occurs at random with respect to environmental perturbations such as climate change, when biogeographical studies show that colonization events in many pathogen clades cluster around climate change perturbations. This contradiction between the traditional paradigm and empirical observations in phylogenetic and real time has been dubbed the *parasite paradox* (Agosta et al., 2010). A new evolutionary framework of host-pathogen associations, the Stockholm paradigm, resolves this paradox.

The Stockholm Paradigm

The Stockholm paradigm (SP) (Brooks et al., 2014; Hoberg and Brooks, 2015; Brooks et al., 2019) is based on two Darwinian principles: (1) **Evolutionary outcomes of interacting species are always local.** All organisms that a pathogen could potentially infect (potential hosts) form its *fundamental fitness space*, while those that the pathogen has actually colonized represent its *realized fitness space*. Coevolutionary processes between the pathogen and a host in a certain geographic locality involve only the realized fitness space and have no effect on other potential hosts in other locations. As a consequence, the smaller the pathogen's realized fitness space is relative to the fundamental fitness space, the higher its potential for colonizing a new host without the need for newly evolved capacities. This potential is referred to as *ecological fitting* (Janzen, 1985). (2) **Evolution is conservative.** All organisms exploit particular resources of their

environment to survive, which requires certain specialized traits. Given these traits are phylogenetically conservative, the same pathogen will be able to utilize and colonize distantly related host species, and, conversely, a novel host will serve as a competent resource for multiple pathogens. Coronaviruses (e.g., SARS, SARS-CoV-2) use receptors distributed across a wide range of Mammalia (Mahdy et al., 2020; Dicken et al., 2021; Lytras et al., 2021), while human red blood cells are targets of various bacterial (*Bartonella bacilliformis*) as well as eukaryotic (*Plasmodium* spp., *Babesia* spp., *Toxoplasma gondii*) pathogens (McCullough, 2014).

Changes in geographical distribution or ecological structure will lead to novel species encounters and provide pathogens with novel opportunities to colonize novel, suitable hosts and increase their realized fitness space (Agosta et al., 2010). Considering genetic variation within the original population, certain low-frequency variants in the original host may be a "better fit" with and thus start rapidly proliferating in the new host. This "stepping-stone dynamic" is a common antecedent of emergences (Araujo et al., 2015; Braga et al., 2015), such as in the 2003 SARS, 2012 MERS, and 2020 SARS-CoV-2 outbreaks (Morens and Fauci, 2020).

Taken together, emergence is not due to the appearance of novel genetic capacities; rather, it is due to the pathogen's taking advantage of new opportunities using preexisting capacities. Pathogens have faced multiple host-range changes throughout their evolutionary history, and each of these events presented them with new suitable hosts they then colonized. The link between climate change and the EID crisis is therefore straightforward and surprisingly simple: changing environmental conditions create movement among species, bringing pathogens in contact with susceptible hosts (Hoberg et al., 2012; Brooks et al., 2019). Pathogens expand their host range and geographic distribution, producing new diversity in these new settings (Hoberg and Brooks, 2015), which set the stage for the next set of emergences, given novel opportunities. Emerging diseases are therefore a built-in feature of evolutionary diversification.

Mobilizing Evolution for Public Health Prevention Efforts

The bad news is that pathogens switch to different hosts frequently during conditions of climate change and globalized trade and travel; therefore, EIDs will continue for an indefinite period of time. The good news is that the conservative nature of genetic capacities makes emergence predictable. The prevailing paradigm used for planning public health policies has linked diseases to the host (and vector) in which they were first found and identified and tries to eliminate that presumed closed cycle (PAHO and WHO, 2008; van den Berg et al., 2012; Cucunubá et al., 2018). Focus is limited to these two target populations, despite overwhelming evidence that any pathogen observed in a host species will be present in numerous sympatric species, even ones distantly related to the original (Parrish et al., 2015; Olivero et al., 2017; Cahan, 2020; Fagre et al., 2021). From a public health perspective, we track the disease to track the pathogen, whereas "the distribution of a pathogen is wider than the disease caused by it, and the latter cannot be understood without understanding the former as a whole" (Audy, 1958). Therefore, even the most organized efforts to eliminate a pathogen from the vector or the host will be faced with an array of reservoirs from which the same pathogen can easily cross over to the newly treated host population, thereby diminishing control efforts in the long term.

The SP offers a way to integrate an evolutionary framework into current disease management strategies to concentrate efforts on preventing emergence. By determining fundamental fitness space as well as observed realized fitness space, we can assign risk to pathogen populations before their emergence. Risk space is maximized along habitat interfaces, where interconnectedness is also increased by climate shifts and human intrusion (Araujo et al., 2015; Brooks et al., 2022). While the ongoing pandemic has all our attention and resources bound by crisis response, the risk spaces for novel EIDs grow by the second. Warming global temperatures and human modified landscapes extend habitable areas for mosquito species such as *Aedes aegypti*, *Aedes albopictus*, or *Anopheles maculipennis*, some of which are competent vectors of malaria, dengue, or yellow fever (Khasnis and Nettleman, 2005; Suzán et al., 2015). Tropical diseases such as chikungunya (Weaver and Lecuit, 2015), dengue (Brady et al., 2012), Zika (Brady and Hay, 2019), and malaria (New map shows, 2018) are constantly reported in Europe, with a large proportion of cases related to travel. Crop diseases such as wheat stem rust (*Puccinia graminis* f. sp. *tritici*) are emerging in crops (Saunders et al., 2019), while the emergent African swine fever virus continues to colonize both swine and wild boar stocks on three continents (Gallardo et al., 2015). Such interfaces and interconnected systems should be primary targets of intensive monitoring with efforts concentrating on tracking pathogens in known reservoirs and alternate vectors. Early interventions should then produce public health, food safety, and wildlife management policies that minimize encounter between reservoirs and susceptible communities, thereby preventing

or mitigating impacts of emergence. In the following section, we describe a four-step prevention protocol that stems from the SP.

Prevent: Predict and Act

Managing risk for EIDs relies on identifying targets for control measures before the onset of a crisis. Strategies thus far have primarily focused on crisis response but have not provided actionable information in advance of an outbreak (Fallah et al., 2015; Daszak et al., 2020; Chatterjee et al., 2021). However, with the accelerating rate of novel emergences, finding them before they find us will be more cost effective than palliation or preparation (Brooks et al., 2019; Brooks et al., 2020; Vianna Franco et al., 2022). Phylogenetically conservative traits make the risk space of EIDs large but also make their behavior predictable in novel settings.

The DAMA protocol—Document, Assess, Monitor, Act—is a comprehensive policy plan stemming directly from the SP (Brooks et al., 2014; Brooks et al., 2019) (Figure 1). It aims to shift the focus of efforts from crisis response (palliation and preparation) to preventing disease outbreaks and facilitating communication between stakeholders in science, health security, and policy making. As well, when prevention is not possible, the DAMA protocol can aid preparation and early response efforts by mitigating the impact of outbreaks.

It is not possible to cope with pathogens without knowing what they are, where they occur, and which potential host species they are likely to infect. **Documenting** pathogens actually or potentially residing in a given region is thus fundamental; strategic inventory feeding into archives for specimens and information is essential (Dunnum et al., 2018). Taking advantage of the evolutionary and ecological context DAMA provides, we focus our search on reservoir hosts. We know that disease-causing organisms of humans, crops, and livestock reside in at least one host that is not diseased. Such reservoirs are often known or suspected, allowing us to

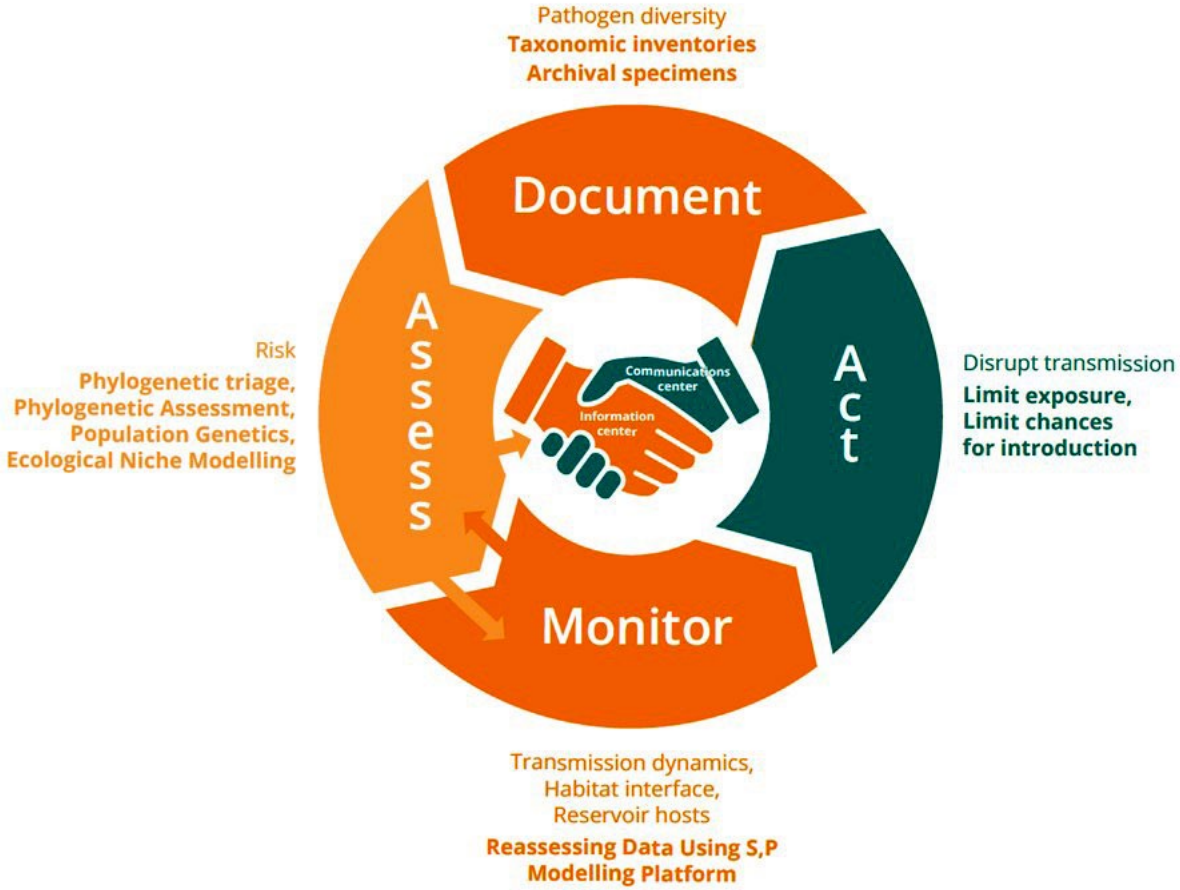

Figure 1. A schematic representation of the DAMA protocol. Keywords next to the circle in normal font represent the overall aim of the respective protocol phase; keywords in bold type describe the methods used to achieve that aim.

focus on a manageable subset of all the species within an area. When reservoirs live in habitats adjacent to human communities or their crops and livestock, disease transmission occurs in the interface between reservoir and human habitats. African swine fever was transmitted from wild boars living around animal breeding facilities to domestic pigs, avian flu spreads through encounters between wild migratory birds and domestic poultry, SARS spread from bats to humans (Cyranoski, 2017). Furthermore, the transmission of pathogens is highly specific for each disease-causing organism—some are transmitted in food, some in water, some by contact between infected hosts or surfaces that have been in contact with infected hosts. Many are transmitted by vectors such as mosquitoes and ticks. Finally, in addition to the information collected during scientific research, local and traditional ecological knowledge from people living in areas at risk is also a significant resource, calling for the establishment of science-society collaboration (Marizzi et al., 2018; Brooks et al., 2019).

Assessing the risk of documented pathogens is a three-step process. The first step is *phylogenetic triage*, which reveals if the species is: (1) known to cause disease in another place, (2) most closely related to non-pathogens, or (3) a close relative of a known pathogen. In the first case, findings should be reported to health authorities; in the second, representative specimens of these species are archived for future reference. In the third case, species are subjected to the second step of risk assessment, *phylogenetic assessment*, using what is known about the close relatives of the novel pathogen to determine possible reservoirs, their mode of transmission, and their microhabitat preferences. Finally, population modeling is done to gather information on population genetics, focusing on the rare genotypes with higher potential to emerge in a new host.

Monitoring pathogens of potential risk begins with detailed mapping of their distribution in areas where they have already been observed as well as searches for them in areas predicted to be suitable. Changes in pathogen populations lead to regular reassessment, while surveillance provides actionable information about changes in risk space before the onset of an epidemic. We are looking for *change*—in geographic distribution, in host range, in transmission dynamics, in geographic variation, in what is there, and in early signs of arrival of anticipated pathogens. A context for comparisons to detect change over time is linked to archival resources and baselines.

Monitoring activities must be rapidly translated into effective **action**. Interventions mainly manifested as policy modifications in the sectors of food safety, wildlife management, veterinary medicine, and public health and education target wildlands, urban/peri-urban, and agricultural landscapes (Trivellone et al., 2022) and interfaces between them. Policies must be generated using historical data stored in natural history biorepositories to accurately evaluate pathogenic and spreading potential of the species in focus. Expertise involved must consider global patterns of trade and travel as well as local environments and community circumstances to maximize feasibility of novel policy developments. Prevention relies on developing interdisciplinary and transdisciplinary networks to determine effective courses of action and coordinate their implementation.

The Prevent-Prepare-Palliate (3P) framework

As demonstrated by the past two decades, one of the biggest threats to modern humanity is the EID crisis, dealing unanticipated damage across all socioeconomic landscapes. Gathering information on symptoms, distribution, and mode of transmission is crucial but not sufficient for avoiding novel emergences. Understanding the novel paradigm describing the ease with which pathogens switch to susceptible host, health security must also shift to a paradigm placing Prevention in the heart of public health. The addition of a preventative element to responses to health threats leads to a tripartite framework of Prevent-Prepare-Palliate (3P) for effective action against EIDs (Figure 2).

In the following sections, we describe different methods for establishing and facilitating communication and information sharing between elements of the framework and within processes of prevention measures.

Communication among the components of the 3P framework

Communication needs to be established between elements of the framework to mutually increase impact. Palliation creates vast knowledge and data on the physiological symptoms caused by particular pathogens, distinguishing between strains and subspecies. The channels to disseminate this information to actors of the prepare element have already been established and provide basis for planning preparatory efforts in case of a resurgence of a known pathogen. However, it is also indispensable knowledge for the prevent element for assessing the risk of a close relative of a known pathogen. Manifestations, treatment options, morbidity, and mortality of a close relative are all taken into consideration when assigning risk to a potential pathogen. The EpiPulse initiative (European Centre for Disease Control and Prevention, 2021) is an exemplary fusion of multiple, distinct surveillance systems for collecting and sharing

Figure 2. Visual representation of the 3P (Prevent-Prepare-Palliate) framework of global health security facing the threat of newly emerging infectious diseases, with examples of organizations and initiatives implementing the prepare and palliate elements.

information on pathogens and facilitating interdisciplinary and cross-sector collaborations.

Preparatory efforts have been substantially improved by adopting the OneHealth approach and thereby including not only medical but also veterinary, agricultural, and wildlife experts in preparing for the onset of a particular disease. Information on reservoirs, vectors, and their distribution are all highly beneficial during phylogenetic assessment of potential pathogens to accurately reveal their range of potential host species. If we expand our target range from the current known pathogens to their close relatives, this tool will prove extremely beneficial in finding them before they find us. An existing hub that allows data entry from diverse sectors' pathogen data stores is the International Nucleotide Sequence Database Collaboration (INSDC) (INSDC, n.d.), an open access data platform under the OneHealth approach (Timme et al., 2020). Information, however, must always be linked back directly to specimens of pathogens and hosts in museums, a process that has not been uniform nor assumed.

Finally, information on high-risk potential pathogens identified by the DAMA protocol will be openly available to preparatory and palliative initiatives, thereby substantially mitigating damages in case of an outbreak.

Communication within the DAMA protocol

The DAMA protocol is designed to combine the techniques of both fundamental and applied research and drive efficient policy making that builds on existing infrastructures and local conditions. The key to such a comprehensive protocol involving stakeholders from multiple different sectors is establishing efficient communication strategies for each of the four phases (Figure 1).

When documenting and assessing pathogens, it is necessary to have globally available linked databases on previously identified and assessed parasitic or microbial organisms and their known host species. To establish baseline conditions of pathogens and all their hosts and reservoirs, specimen sourcing has to be followed by permanent archiving. Implementing standardized entry protocols; collaborative, directed collection efforts; and

globally accessible databases provides opportunity for detecting pathogenic microbes in their reservoirs before host switching can result in human cases. Establishing baseline conditions is then followed by periodic resampling to monitor changes in distribution, genetic composition, and host range. Although calls for creating global repositories and archives have been made previously (Brooks and Hoberg, 2000), large-scale collection efforts have failed to permanently archive their specimens in biorepositories (Kelly et al., 2017; Grange et al., 2021), depriving further studies from the valuable data that were collected at high monetary cost.

Colella et al. (2021) recently proposed that biorepositories, such as those mentioned in the Global Museum initiative (Bakker et al., 2020), present a possible solution for archiving and cataloging potential pathogens along with their reservoirs to build cohesive informatics resources that describe diversity (Dunnum et al., 2018). Biorepositories include in their collections substantial numbers of individual vertebrates and invertebrates that can be and often are screened for the potential pathogens that may occur in archived specimens. Parasites or pathogens detected in these archival collections can then be used as alerts and as starting points for additional field-based studies.

Traditional disease surveillance is either limited by jurisdictional boundaries or comes at a significantly higher cost for larger-scale monitoring (Palmer et al., 2017), both of which limit public health security. The DAMA protocol relies heavily on effective working relationships with local communities, involving members in not only collecting data but also gathering traditional insights and observations regarding reservoirs. Establishing communication channels and training programs between susceptible communities and public health authorities will foster trust in science and allow for a close collaboration with those affected when planning and implementing intervention measures and novel policies. Grassroots-level science has been successfully employed in tracking mosquito and tick vectors (Palmer et al., 2017; Földvári et al., 2022), monitoring avian flu in urban environments (Marizzi et al., 2018; Szekeres et al., 2019), and surveying wildlife health (Lawson et al., 2015), creating the dual benefit of access to larger data and increased awareness in communities at high risk of emergence. Such initiatives are also designed to become bases for long-term science-practice collaboration in their respective localities.

Finally, designing effective *action* in light of information gathered in the previous three phases warrants the close cooperation of various governmental, municipal, scientific, and local stakeholders. A promising approach is adopting the innovative Living Lab methodology (Herrera, 2017; Steen and van Bueren, 2017; Huang and Thomas, 2021) into the context of disease management by establishing multi-actor consensus groups that consist of various regional stakeholders impacted by an emerging disease. The Living Lab method aims to increase the efficiency of implementing novel achievements into real-life contexts by inviting all stakeholders into a collaborative task force (Veeckman et al., 2013). Consensus groups consist of scientific personnel as well as public health policy experts, regional governmental officials, and members of the exposed populations. The aim of this method is for all actors to jointly analyze the issue at hand; identify the implications an emerging pathogen has for residential, legal, healthcare, and scientific landscapes; and then cooperate in designing an efficient and highly adoptable intervention plan, which takes into account not only wider scientific context but also regional policy environments and local feasibility. Although Living Lab methodology presents multiple challenges in terms of implementation, it has been successfully applied in monitoring health states of elderly patients (Kim et al., 2020) and addressing neurological issues (Richardson et al., 2021). The apparent suitability for addressing noncommunicable diseases strongly suggests the methodology should be introduced into the context of infectious disease management as well.

The fact that the health-science and scientific community has thus far failed to decrease the number of novel emergences is explained mainly by the lack of effective communication among inter- and trans-disciplinary systems. Cutting-edge research in studies of evolution of pathogens is not contextualized in veterinary science, agriculture, or public health, and implications of evolutionary processes are not considered during policy making.

Disseminating the importance of reducing exposure and monitoring early warning signs and planning interventions to prevent, not merely contain, outbreaks is the only way to strengthen global health security.

Conclusions

EIDs affect every layer of modern society on local to global scales (Kapiriri and Ross, 2020). Reducing the impacts of EID through prevention rather than crisis response is the key to a sustainable future for humanity. The emergence of another pandemic is not a question of if but when and where. The DAMA protocol is necessary for addressing the EID crisis and requires the interdisciplinary collaboration of experts in healthcare policy, epidemiology, and pathogen-host evolution. Efforts have to focus on maintaining the guiding principle of anticipatory action while also integrating the novel approach

into existing frameworks and programs. DAMA can help us buy time and save resources in the global effort to cope with the EID crisis. The Prevent-Prepare-Palliate framework clarifies aims and goals of health security initiatives, allowing existing infrastructure to focus on mitigating the impacts of EID that have already emerged, while preventing new EID and mitigating the impacts of those that cannot be prevented. Global climate change and globalized trade and travel create new challenges, and our efforts to cope can and must adapt.

We know what to do, we have the tools and the expertise, and the next step is to implement the DAMA protocol before the next pandemic. Global health security relies on a complex network of institutions and organizations operating in various policy environments and accommodating diverse scientific inputs. Therefore, the emphasis must now be on establishing cross-sector communication channels by (1) creating globally accessible databanks that accommodate input from different scientific fields and public sectors and can be used by disease management to assess risk of potential pathogens, (2) involving grassroots-level contributors in research studies to facilitate communication and trust between public health and susceptible communities, and (3) employing cutting-edge approaches such as the Living Lab method to include all stakeholders in generating solutions to the EID threat.

* * *

Acknowledgments – The authors thank Adél Marx for her help in collecting and reviewing literature and Mátyás Massár for assistance with visualization tools. DRB thanks the Hungarian Academy of Sciences for support during March–May 2022 as part of the program MTA Distinguished Guest Fellowship in Hungary.

Conflict of Interest – The authors declare that they have no conflicts of interest.

Author Contribution Statement – *O. Molnár:* Conceptualization (lead), Investigation (lead), Supervision (equal), Visualization (lead), Writing—Original Draft Preparation (lead), Writing—Review & Editing (equal); *E. Hoberg:* Conceptualization (supporting), Writing—Review & Editing (equal); *V. Trivellone:* Writing—Review & Editing (equal); *G. Foldvári:* Writing—Review & Editing (equal); and *D. R. Brooks:* Supervision (equal), Writing—Original Draft Preparation (supporting), Writing—Review & Editing (equal).

References

Agosta, S. J.; Janz, N.; Brooks, D. R. 2010. How specialists can be generalists: resolving the and "parasite paradox" and implications for emerging infectious disease. Zoologia 27: 151–162. https://doi.org/10.1590/51984-46702010000200001

Apari, P.; Bajer, K.; Brooks, D.R.; Molnár, O. 2019. Hiding in plain sight: an evolutionary approach to the South American Zika outbreak and its future consequences. Zoologia 36: 1–7. https://doi.org/10.3897/zoologia.36.e36272

Araujo, S.B.L.; Braga, M.P.; Brooks, D.R.; Agosta, S.J.; Hoberg, E.P.; von Hartenthal, F.W.; Boeger, W.A. 2015. Understanding host-switching by ecological fitting. PloS ONE 10: e0139225. https://doi.org/10.1371/journal.pone.0139225

Audy, J.R. 1958. The localization of disease with special reference to the zoonoses. Transactions of the Royal Society of Tropical Medicine and Hygiene 52: 308-334. https://doi.org/10.1016/0035-9203(58)90045-2

AVMA [American Veterinary Medical Association]. 2008. One Health: A New Professional Imperative. One Health Initiative Task Force : Final Report, July 15, 2008. https://www.avma.org/resources-tools/reports/one-health-ohitf-final-report-2008

Bakker, F.T.; Antonelli, A.; Clarke, J.A.; Cook, J.A.; Edwards, S.V.; Ericson, P.G.P.; et al. 2020. The Global Museum: natural history collections and the future of evolutionary science and public education. PeerJ 8: e8225. https://doi.org/10.7717/peerj.8225

Bill & Melinda Gates Foundation. n.d. Bill & Melinda Gates Foundation (website). Accessed August 18, 2021. https://www.gatesfoundation.org/

Blake, P.; Wadhwa, D. 2020. 2020 Year in Review: The Impact of COVID-19 in 12 Charts. Accessed October 12, 2021. https://blogs.worldbank.org/voices/2020-year-review-impact-covid-19-12-charts

Bowden, M.E.; Crow, A.B.; Sullivan, T. 2003. Pharmaceutical Achievers: The Human Face of Pharmaceutical Research. Chemical Heritage Foundation, Philadelphia. 214 pp.

Brady, O.J.; Gething, P.W.; Bhatt, S.; Messina, J.P.; Brownstein, J.S.; Hoen, A.G.; et al. 2012. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. PLoS Neglected Tropical Diseases 6: e1760. https://doi.org/10.1371/journal.pntd.0001760

Brady, O.J.; Hay, S.I. 2019. The first local cases of Zika virus in Europe. The Lancet 394: 1991–1992. https://doi.org/10.1016/S0140-6736(19)32790-4

Braga, M.P.; Razzolini, E.; Boeger, W.A. 2015. Drivers of parasite sharing among neotropical freshwater fishes. Journal of Animal Ecology 84: 487–497. https://doi.org/10.1111/1365-2656.12298

Breiman, R.F. 1996. Impact of technology on the emergence of infectious diseases. Epidemiologic Reviews 18: 4–9. https://doi.org/10.1093/oxfordjournals.epirev.a01791

Brooks, D.R.; Ferrao, A.L. 2005. The historical biogeography of co-evolution: emerging infectious diseases are evolutionary accidents waiting to happen. Journal of Biogeography 32: 1291–1299. https://doi.org/10.1111/j.1365-2699.2005.01315.x

Brooks, D.R.; Hoberg, E.P. 2000. Triage for the biosphere: the need and rationale for taxonomic inventories and phylogenetic studies of parasites. Comparative Parasitology 67: 1–25.

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A. 2019. The Stockholm Paradigm: Climate Change and Emerging Disease. University of Chicago Press, Chicago.

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A.; Gardner S.L.; Araujo, S.B.L.; Bajer, K.; et al. 2020. Before the pandemic ends: making sure this never happens again. World Complexity Science Academy Journal 1: 8. https://doi.org/10.46473/wcsaj27240606/15-05-2020-0002//full/html

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A.; Gardner, S.L.; Galbreath, K.E.; Herczeg, D.; et al. 2014. Finding them before they find us: informatics, parasites, and environments in accelerating climate change. Comparative Parasitology 81: 155–164. https://doi.org/10.1654/4724b.1

Brooks, D.R.; Hoberg, E.P.; Boeger, W.A.; Trivellone, V. 2022. Emerging infectious disease: an underappreciated area of strategic concern for food security. Transboundary and Emerging Diseases 69: 254–267. https://doi.org/10.1111/tbed.14009

Burkle, F.M., Jr.; Burkle, C.M. 2015. Triage management, survival, and the law in the age of Ebola. Disaster Medicine and Public Health Preparedness 9: 38–43. https://doi.org/10.1017/dmp.2014.117

Burns, A.; van der Mensbrugghe, D.; Timmer, H. 2008. Evaluating the Economic Consequences of Avian Influenza. The World Bank [working paper]. Accessed September 24, 2022. https://documents.worldbank.org/en/publication/documents-reports/documentdetail/977141468158986545/evaluating-the-economic-consequences-of-avian-influenza

Cahan, E. 2020 Aug 18. COVID-19 hits U.S. mink farms after ripping through Europe. Science. https://doi.org/10.1126/science.abe3870

Centers for Disease Control and Prevention. 2022. Avian Influenza in Birds. Accessed November 2, 2021. https://www.cdc.gov/flu/avianflu/avian-in-birds.htm

Chatterjee, P.; Nair, P.; Chersich, M.; Terefe, Y.; Chauhan, A.S.; Quesada, F.; Simpson, G. 2021. One Health, "Disease X" and the challenge of "unknown" unknowns. Indian Journal of Medical Research 153: 264–271. https://doi.org/10.4103/ijmr.IJMR_601_21

Colella, J.P.; Bates, J.; Burneo, S.F.; Camacho, M.A.; Bonilla, C.C.; Constable, I.; et al. 2021. Leveraging natural history biorepositories as a global, decentralized, pathogen surveillance network. PLoS Pathogens 17: e1009583. https://doi.org/10.1371/journal.ppat.1009583

Cucunubá, Z.M.; Nouvellet, P.; Peterson, J.K.; Bartsch, S.M.; Lee, B.Y.; Dobson, A.P.; Basáñez, M.-G. 2018. Complementary paths to Chagas disease elimination: the impact of combining vector control with etiological treatment. Clinical Infectious Diseases 66: S293–S300. https://doi.org/10.1093/cid/ciy006

Cyranoski, D. 2017. Bat cave solves mystery of deadly SARS virus—and suggests new outbreak could occur. Nature 552: 15–16. https://doi.org/10.1038/d41586-017-07766-9

Daszak, P.; Olival, K.J.; Li, H. 2020. A strategy to prevent future epidemics similar to the 2019-nCoV outbreak. Biosafety and Health 2: 6–8. https://doi.org/10.1016/j.bsheal.2020.01.003

Datt, N.; Gosai, R.C.; Raviwasa, K.; Timote, V. 2020. Key transboundary plant pests of coconut [*Cocos nucifera*] in the Pacific Island Countries—a biosecurity perspective. Plant Pathology & Quarantine 10: 152–171. https://doi.org/10.5943/ppq/10/1/17

DeSalvo, K.; Hughes, B.; Bassett, M.; Benjamin, G.; Fraser, M.; Galea, S.; et al. 2021. Public health COVID-19 impact assessment: lessons learned and compelling needs. NAM Perspectives. https://doi.org/10.31478/202104c

Dicken, S.J.; Murray, M.J.; Thorne, L.G.; Reuschl, A.-K.; Forrest, C.; Ganeshalingham, M.; et al. 2021. Characterisation of B.1.1.7 and Pangolin coronavirus spike provides insights on the evolutionary trajectory of SARS-CoV-2. bioRxiv preprint. https://doi.org/10.1101/2021.03.22.436468

Dunnum, J.L.; McLean, B.S.; Dowler, R.C.; Systematic Collections Committee of the American Society of Mammalogists. 2018. Mammal collections of the Western Hemisphere: a survey and directory of collections. Journal of Mammalogy 99: 1307–1322. https://doi.org/10.1093/jmammal/gyy151

EcoHealth Alliance. n.d. Scientific Research and Pandemic Prevention. Accessed September 13, 2021. https://www.ecohealthalliance.org/

European Centre for Disease Prevention and Control. 2021. EpiPulse—the European surveillance portal for infectious diseases. Accessed March 22, 2022. https://www.ecdc.europa.eu/en/publications-data/epipulse-european-surveillance-portal-infectious-diseases

Evans, M.R. 2010. The swine flu scam? Journal of Public Health 32: 296–297. https://doi.org/10.1093/pubmed/fdq059

Fagre, A.C.; Lewis, J.; Miller, M.R.; Mossel, E.C.; Lutwama, J.J.; et al. 2021. Subgenomic flavivirus RNA (sfRNA) associated with Asian lineage Zika virus identified in three species of Ugandan bats (family Pteropodidae). Scientific Reports 11: 8370. https://doi.org/10.1038/s41598-021-87816-5

Fallah, M.; Skrip, L.A.; d'Harcourt, E.; Galvani, A.P. 2015. Strategies to prevent future Ebola epidemics. The Lancet 386: 131. https://doi.org/10.1016/S0140-6736(15)61233-8

FAO [Food and Agriculture Organization of the United Nations]. 2019. Food Outlook: Biannual Report on Global Food Markets, November 2019. Rome.

FAO; OiE; WHO [Food and Agriculture Organization of the United Nations; World Organisation for Animal Health; World Health Organization]. 2006. Global Early Warning and Response System for Major Animal Diseases, Including Zoonoses (GLEWS). https://www.woah.org/fileadmin/Home/eng/About_us/docs/pdf/GLEWS_Tripartite-Finalversion010206.pdf

Földvári, G.; Szabó, É.; Tóth, G.E.; Lanszki, Z.; Zana, B.; Varga, Z.; Kemenesi, G. 2022. Emergence of *Hyalomma marginatum* and *Hyalomma rufipes* adults revealed by citizen science tick monitoring in Hungary. Transboundary and Emerging Diseases 69: e2240–e2248. https://doi.org/10.1111/tbed.14563

Foster, J.B.; Clark, B.; Holleman, H. 2021. Capital and the ecology of disease. Monthly Review 73: 1–23. https://doi.org/10.14452/MR-073-02-2021-06_1

Gallardo, M.C.; de la Torre Reoyo, A.; Fernández-Pinero, J.; Iglesias, I.; Muñoz, M.J.; Arias, M.L. 2015. African swine fever: a global view of the current challenge. Porcine Health Management 1: 21. https://doi.org/10.1186/s40813-015-0013-y

GISRS [Global Influenza Surveillance and Response System]. n.d. GISRS (website). World Health Organization. Accessed August 17, 2021. https://www.who.int/initiatives/global-influenza-surveillance-and-response-system

GOARN [Global Outbreak Alert and Response Network]. n.d. GOARN [website]. World Health Organization. Accessed August 17, 2021. https://extranet.who.int/goarn/

Grange, Z.L.; Goldstein, T.; Johnson, C.K.; Anthony, S.; Gilardi, K.; Daszak, P.; et al. 2021. Ranking the risk of animal-to-human spillover for newly discovered viruses. Proceedings of the National Academy of Sciences USA 118: e2002324118. https://doi.org/10.1073/pnas.2002324118

Gurr, G.M.; Johnson, A.C.; Ash, G.J.; Wilson, B.A.L.; Ero, M.M.; Pilotti, C.A.; et al. 2016. Coconut lethal yellowing diseases: a phytoplasma threat to palms of global economic and social significance. Frontiers in Plant Science 7: 1521. https://doi.org/10.3389/fpls.2016.01521

Hadler, J.L.; Patel, D.; Nasci, R.S.; Petersen, L.R.; Hughes, J.M.; Bradley, K.; et al. 2015. Assessment of arbovirus surveillance 13 years after introduction of West Nile virus, United States. Emerging Infectious Diseases 21: 1159–1166. https://doi.org/10.3201/eid2107.140858

Herrera, N.R. 2017. The emergence of living lab methods. In: Living Labs: Design and Assessment of Sustainable Living. D.V. Keyson, O. Guerra-Santin, D. Lockton (eds.). Springer, Berlin/Heidelberg.

Hoberg, E.P.; Brooks, D.R. 2015. Evolution in action: climate change, biodiversity dynamics and emerging infectious disease. Philosophical Transactions of the Royal Society B: Biological Sciences 370: 20130553. https://doi.org/10.1098/rstb.2013.0553

Hoberg, E.P.; Galbreath, K.E.; Cook, J.A.; Kutz, S.J.; Polley, L. 2012. Northern host-parasite assemblages: history and biogeography on the borderlands of episodic climate and environmental transition. In: Advances in Parasitology 79. D. Rollinson and S.I. Hay (eds.). Elsevier, Amsterdam. 1–97 p. https://doi.org/10.1016/B978-0-12-398457-9.00001-9

Huang, J.H.; Thomas, E. 2021. A review of living lab research and methods for user involvement. Technology Innovation Management Review 11: 88–107. http://doi.org/10.22215/timreview/1467

ILO [International Labour Organization]. 2021. World Employment and Social Outlook: Trends 2021. International Labour Office, Geneva. 161 pp. https://www.ilo.org/global/research/global-reports/weso/2021/WCMS_795453/lang--en/index.htm

INSDC [International Nucleotide Sequence Database Collaboration]. n.d. INSDC (website). Accessed March 22, 2022. https://www.insdc.org/

Jacobs, L.A. 2007. Rights and quarantine during the SARS global health crisis: differentiated legal consciousness in Hong Kong, Shanghai, and Toronto. Law and Society Review 41: 511–552. https://doi.org/10.1111/j.1540-5893.2007.00313.x

Janzen, D.H. 1985. On ecological fitting. Oikos 45: 308–310. https://doi.org/10.2307/3565565

Johns Hopkins Center for Civilian Biodefense Studies, Center for Strategic and International Studies, ANSER Institute for Homeland Security, and National Memorial Institute for the Prevention of Terrorism. 2001. Dark Winter: Bioterrorism Exercise, Andrews Air Force Base, June 22–23, 2001. Final Script, Explanatory Note to the Exercise Script, p. 2. Accessed https://carterheavyindustries.files.wordpress.com/2020/05/dark-winter-script.pdf

Kapiriri, L.; Ross, A. 2020. The politics of disease epidemics: a comparative analysis of the SARS, Zika, and Ebola outbreaks. Global Social Welfare 7: 33–45. https://doi.org/10.1007/s40609-018-0123-y

Kelly, T.R.; Karesh, W.B.; Johnson, C.K.; Gilardi, K.V.K.; Anthony, S.J.; Goldstein, T.; et al. 2017. One Health proof of concept: bringing a transdisciplinary approach to surveillance for zoonotic viruses at the human–wild animal interface. Preventive Veterinary Medicine 137 (Part B): 112–118. https://doi.org/10.1016/j.prevetmed.2016.11.023

Khasnis, A.A.; Nettleman, M.D. 2005. Global warming and infectious disease. Archives of Medical Research 36: 689–696. https://doi.org/10.1016/j.arcmed.2005.03.041

Khoo, E.J.; Lantos, J.D. 2020. Lessons learned from the COVID-19 pandemic. Acta Paediatrica 109: 1323–1325. https://doi.org/10.1111/APA.15307

Kim, J.; Kim, Y.L.; Jang, H.; Cho, M.; Lee, M.; Kim, J.; Lee, H.; et al. 2020. Living labs for health: an integrative literature review. European Journal of Public Health 30: 55–63. https://doi.org/10.1093/eurpub/ckz105

Lakoff, A. 2017. Unprepared: Global Health in a Time of Emergency. University of California Press, Oakland. 240 p.

Lane, H.J.; Blum, N.; Fee, E. 2010. Oliver Wendell Holmes (1809–1894) and Ignaz Philipp Semmelweis (1818–1865): preventing the transmission of puerperal fever. American Journal of Public Health 100: 1008–1009. https://doi.org/10.2105/AJPH.2009.185363

Lawson, B.; Petrovan, S.O.; Cunningham, A.A. 2015. Citizen science and wildlife disease surveillance. EcoHealth 12: 693–702. https://doi.org/10.1007/s10393-015-1054-z

Leach, M.; Dry, S. 2010. Epidemics: Science, Governance and Social Justice. Routledge, Oxfordshire, England. 320 pp.

Lytras, S.; Xia, W.; Hughes, J.; Jiang, X.; Robertson, D.L. 2021. The animal origin of SARS-CoV-2. Science 373: 968–970. https://doi.org/10.1126/science.abh0117

Mahdy, M.A.A.; Younis, W.; Ewaida, Z. 2020. An overview of SARS-CoV-2 and animal infection. Frontiers in Veterinary Science 7: 596391. https://doi.org/10.3389/fvets.2020.596391

Marizzi, C.; Florio, A.; Lee, M.; Khalfan, M.; Ghiban, C.; Nash, B.; et al. 2018. DNA barcoding Brooklyn (New York): a first assessment of biodiversity in Marine Park by citizen scientists. PLoS ONE 13: e0199015. https://doi.org/10.1371/journal.pone.0199015

Martinez, A.P.; Roberts, D.A. 1967. Lethal yellowing of coconuts in Florida. Proceedings of the Florida State Horticultural Society 80: 432.

McCullough, J. 2014. RBCs as targets of infection. Hematology 2014: 404–409. https://doi.org/10.1182/asheducation-2014.1.404

Morens, D.M.; Fauci, A.S. 2020. Emerging pandemic diseases: how we got to COVID-19. Cell 182: 1077–1092. https://doi.org/10.1016/j.cell.2020.08.021

MSF [Médecins Sans Frontières]. n.d. MSF (website). Accessed August 18, 2021. https://www.msf.org/

New map shows the presence of *Anopheles maculipennis* s.l. mosquitoes in Europe. 2018. European Centre for Disease Prevention and Control. Accessed November 29, 2021. https://www.ecdc.europa.eu/en/news-events/new-map-shows-presence-anopheles-maculipennis-sl-mosquitoes-europe

Newton, J.; Kuethe, T. 2015. Economic implications of the 2014–2015 bird flu. farmdoc daily 5: 104, Department of Agricultural and Consumer Economics, University of Illinois at Urbana-Champaign.

Olivero, J.; Fa, J.E.; Real, R.; Farfán, M.Á.; Márquez, A.L.; Vargas, J.M.; et al. 2017. Mammalian biogeography and the Ebola virus in Africa. Mammal Review 47: 24–37. https://doi.org/10.1111/mam.12074

PAHO; WHO [Pan American Health Organization and World Health Organization]. 2008. Resolution CD48. R8: Integrated Vector Management: A Comprehensive Response to Vector-borne Diseases. 48th Directing Council, 60th Session of the Regional Committee, Washington, DC, USA, September 29–October 3, 2008. 3 pp. https://www3.paho.org/english/gov/cd/cd48.r8-e.pdf

Palmer, J.R.B.; Oltra, A., Collantes, F.; Delgado, J.A.; Lucientes, J.; Delacour, S.; et al. 2017. Citizen science provides a reliable and scalable tool to track disease-carrying mosquitoes. Nature Communications 8: 916. https://doi.org/10.1038/s41467-017-00914-9

Parrish, C.R.; Kawaoka, Y. 2005. The origins of new pandemic viruses: the acquisition of new host ranges by canine parvovirus and influenza A viruses. Annual Review of Microbiology 59: 553–586. https://doi.org/10.1146/annurev.micro.59.030804.121059

Parrish, C.R.; Murcia, P.R.; Holmes, E.C. 2015. Influenza virus reservoirs and intermediate hosts: dogs, horses, and new possibilities for influenza virus exposure of humans. Journal of Virology 89: 2990–2994. https://doi.org/10.1128/jvi.03146-14

Plourde, A.R.; Bloch, E.M. 2016. A literature review of Zika virus. Emerging Infectious Diseases 22: 1185–1192. https://doi.org/10.3201/eid2207.151990

Richardson, S.; Sinha, A.; Vahia, I.; Dawson, W.; Kaye, J.; et al. 2021. Brain health living labs. American Journal of Geriatric Psychiatry 29: 698–703. https://doi.org/10.1016/j.jagp.2020.11.010

Rohde, K., ed. 2013. The Balance of Nature and Human Impact. Cambridge University Press, Cambridge, England.

Saunders, D.G.O.; Pretorius, Z.A.; Hovmøller, M.S. 2019. Tackling the re-emergence of wheat stem rust in Western Europe. Communications Biology 2: 51. https://doi.org/10.1038/s42003-019-0294-9

Steen, K.; van Bueren, E. 2017. Urban Living Labs: A Living Lab Way of Working. Amsterdam Institute for Advanced Metropolitan Solutions, Delft University of Technology. 95 pp. https://research.tudelft.nl/en/publications/urban-living-labs-a-living-lab-way-of-working

Stenseth, N.C.; Dharmarajan, G.; Li, R.; Shi, Z.L.; Yang, R.; Gao, G.F. 2021. Lessons learnt from the COVID-19 pandemic. Frontiers in Public Health 9: 694705. https://doi.org/10.3389/fpubh.2021.694705

Suzán, G.; García-Peña, G.E.; Castro-Arellano, I.; Rico, O.; Rubio, A.V.; Tolsá, M.J.; et al. 2015. Metacommunity and phylogenetic structure determine wildlife and zoonotic infectious disease patterns in time and space. Ecology and Evolution 5: 865–873. https://doi.org/10.1002/ece3.1404

Szekeres, S.; Docters van Leeuwen, A.; Tóth, E.; Majoros, G.; Sprong, H.; Földvári, G. 2019. Road-killed mammals provide insight into tick-borne bacterial pathogen communities within urban habitats. Transboundary and Emerging Diseases 66: 277–286. https://doi.org/10.1111/tbed.13019

Timme, R.E.; Wolfgang, W.J.; Balkey, M.; Gubbala Venkata, S.L.; Randolph, R.; Allard, M.; Strain, E. 2020. Optimizing open data to support One Health: best practices to ensure interoperability of genomic data from bacterial pathogens. One Health Outlook 2: 20. https://doi.org/10.1186/s42522-020-00026-3

Trivellone, V.; Hoberg, E.P.; Boeger, W.A.; Brooks, D.R. 2022. Food security and emerging infectious disease: risk assessment and risk management. Royal Society Open Science 9: 211687. https://doi.org/10.1098/rsos.211687

van den Berg, H.; Zaim, M.; Singh Yadav, R.; Soares, A.; Ameneshewa, B.; Mnzava, A.; et al. 2012. Global trends in the use of insecticides to control vector-borne diseases. Environmental Health Perspectives 120: 577–582. https://doi.org/10.1289/ehp.1104340

Veeckman, C.; Schuurman, D.; Leminen, S.; Westerlund, M. 2013. Linking living lab characteristics and their outcomes: towards a conceptual framework. Technology Innovation Management Review 3: 6–15. https://doi.org/10.22215/timreview748

Vianna Franco, M.P.; Molnár, O.; Dorninger, C.; Laciny, A.; Treven, M.; Weger, J.; et al. 2022. Diversity regained: precautionary approaches to COVID-19 as a phenomenon of the total environment. Science of the Total Environment 825: 154029. https://doi.org/10.1016/j.scitotenv.2022.154029

Weaver, S.C.; Lecuit, M. 2015. Chikungunya virus and the global spread of a mosquito-borne disease. New England Journal of Medicine 372: 1231–1239. https://doi.org/10.1056/nejmra1406035

WHO [World Health Organization]. 2020. The COVID-19 Pandemic: Lessons Learned for the WHO European Region: A Living Document, 15 September 2020. https://apps.who.int/iris/handle/10665/334385

WHO [World Health Organization]. 2007. The World Health Report 2007: A Safer Future: Global Public Health Security in the 21st Century. WHO Press, Geneva, Switzerland. 72 pp. https://www.who.int/publications/i/item/9789241563444

WHO [World Health Organization]. 2005. International Health Regulations (2005). 3rd ed. WHO Press, Geneva, Switzerland. 74 pp. https://www.who.int/publications/i/item/9789241580496

WHO; World Bank [World Health Organization and International Bank for Reconstruction and Development/The World Bank]. 2019. Global Monitoring Report on Financial Protection in Health 2019. 50 pp. https://www.who.int/publications/i/item/9789240003958